

The Development of Specialization in Allergy

A Historical Review and a View Ahead

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ON MARCH 18, 1819, Dr. John Bostock,⁴ an English physiologist and clinician, read a paper before the Royal Medical and Chirurgical Society of London on a Case of a Periodic Affection of the Eyes and Chest, in which he presented to the members the history and clinical symptoms of a seasonal affection which had troubled him since childhood.

In January 1922, the American Association for the Study of Allergy was organized in San Francisco, and held its first meeting in June 1923. In March of the same year, an organizational meeting was held in the City of New York, which resulted in the founding of the Society for the Study of Asthma and Allied Conditions. The amalgamation of these two organizations in 1943 to form the Academy of Allergy, and the founding during the previous year of the American College of Allergists, served to bring all workers in clinical allergy together in the pursuit of a common objective.

The hundred year period from the clinical observations of Bostock to the organized efforts of many students of allergy covers the major contributions which have led to the recognition of allergy as a clinical entity and the development of specialization in study and treatment of the condition.

It was Carlyle who expressed the view that history is the essence of innumerable biographies and that anyone who wishes to know the history of any period must know the men who made it what it was. Although medical history is concerned more with ideas than with biography, the acceptance or rejection of an idea, particularly prior to the development of the experimental method, was determined in no small measure by the personality and reputation of the physician who advanced the idea. The historical development of interest in allergy as a clinical subject bears out this point.

John Elliotson, a contemporary of Bostock, in a clinical lecture delivered at St. Thomas Hospital in London on March 31, 1831,⁹ made the first definite suggestion that hay fever depends on the flower of grass and probably upon the pollen. When the lecture was delivered, Elliotson was at the height of his career as a teacher and consultant in London.

•Clinical allergy as a special field of practice is a little more than twenty-five years old. The organized efforts of the two national societies for the study of allergy and the many county, state and regional groups of physicians interested in allergic diseases have served to bring all workers in the field together in pursuit of a common objective. However, the foundation stones for the specialty were laid by a number of astute clinical observers during the past hundred years.

This historical sketch aims to portray these men and their work, and points out how the introduction of the skin test as a diagnostic method has dominated the clinical approach to allergic diseases during the past half-century—and that the technique is gradually losing some of its significance. This changing emphasis from the older diagnostic procedures to other techniques is the result of the discovery of the new hormones, cortisone and corticotropin (ACTH). These hormones have presented another method of studying the mechanism of allergic phenomena in man. Finally, brief reference is made to the growing recognition of the significance of the psychosomatic factors in the management of the allergic patient and the influence of this and the other additions to knowledge on the training of the future generations of allergists.

His great industry, acknowledged abilities and prepossessing manners made it possible for him to forge ahead in London. A year after his graduation from Cambridge in 1821, he was elected physician to St. Thomas Hospital, where he became the most energetic teacher of the day. His lectures on hay fever are of particular interest to students of allergy because Elliotson was probably the first to mention the occurrence of dermatitis of the hands following the handling of the flower of grass. In referring to this observation, he wrote: "On handling the flower of grass, her hands always became instantly inflamed; therefore there is clearly in her skin a peculiar susceptibility of irritation from the flowers

⁴Chairman's Address. Presented before the Section on Allergy at the 81st Annual Session of the California Medical Association, Los Angeles, April 27-30, 1952.

of grass." And he concluded, "I presume that the same morbid state exists in the mucous membranes."

This keen observer also anticipated by a quarter of a century Hyde Salter's classical description of hay fever and asthma following exposure to animal epidermal substances.¹³ Of a woman patient sensitive to rabbits, Elliotson wrote that proximity to rabbits "produced a running at the nose and eyes and soreness of the upper lip; that if she went into a place where there were rabbits, it came on; and that if her husband came in after having shot a rabbit and threw it down near her, those effects were instantly produced."⁹

The great error of Elliotson's life was the espousal of mesmerism. In 1843, he published a pamphlet describing "Numerous Cases of Surgical Operations Without Pain in the Mesmeric State." His wards became filled with hysterical and excitable women, who were magnetized to sleep in order to try the effects of the new remedy, the fame of which had spread far and wide. Because of these activities, Elliotson fell into disfavor and with him the original and brilliant clinical observations on hay fever which he made. Knowledge of the underlying cause of hay fever was thereby retarded by almost fifty years.

In 1873, Charles Harrison Blackley of Manchester, England, published his "Experimental Researches on the Causes and Nature of Catarrhus Aestivus (Hay Fever)," and in 1880 appeared his more complete work entitled "Hay Fever, Its Causes, Treatment and Effective Prevention." Of his own case and the circumstances which led up to his ingenious experiments on hay fever, Blackley wrote: "I have, as I have previously said, suffered from hay fever for more than twenty-five years, but the exact time at which the disorder first commenced, I cannot now remember. The attacks lasted only a few days, and then declined rapidly; and they seemed then to me, to be in some way dependent upon the commencement of warm weather."²

The well-controlled experimental observations of Blackley and the accuracy of his deductions from them are indeed remarkable when viewed in the light of present knowledge of hay fever, particularly since his work was done before the controlled experiment had come into general use in medicine. Being subject to the disease, Blackley tested on himself the pollen of nearly one hundred different species of grasses and flowers, in the fresh as well as in the dried state and also, in some instances, in the form of alcoholic extracts. Five different ways of testing the pollen were tried: "(1) by applying it to the mucous membranes of the nares; (2) by inhaling it, and thus bringing it into contact with the mucous membranes of the larynx, trachea, and bronchial tubes; (3) by applying a decoction of

the pollen to the conjunctiva; (4) by applying the fresh pollen to the tongue, lips, and fauces; (5) by inoculating the upper and lower limbs with the fresh moistened pollen."²

Thus it appears that Blackley anticipated by more than a quarter of a century the use of the diagnostic scratch and mucous membrane tests for pollen sensitivity. Of his use of the skin test, he wrote: "Whilst I was still suffering from my usual attack of hay fever, during the summer of 1865, as much pollen as could be obtained from two anthers of the *Lolium italicum* was applied to the center of the anterior surface of the forearm after the skin had been abraded, and to this the quantity of pollen named was applied after being placed on a piece of wet lint the size of the abrasion. This was covered with a piece of gutta percha, and the whole was held in position by a strip of adhesive plaster. The center of the other forearm was treated in exactly the same manner save and except that no pollen was applied to it. The scratching with the lancet raised a wheal such as is seen in urticaria or in the stinging with nettles. In a few minutes after the pollen had been applied the abraded spot began to itch intensely; the parts immediately around the abrasion began to swell, but this was apparently not due to any action on the cutis vera. In the above experiment the swelling seemed to be entirely due to effusion into the subcutaneous cellular tissues. The swelling attained its maximum in six hours, and then remained stationary for another eight hours. After this it gradually subsided, and in forty-eight hours, it had entirely disappeared. The arm to which no pollen had been applied did not exhibit any sign of swelling or irritation."²

Having established that seasonal hay fever is caused by pollen, Blackley undertook a series of experiments to find the quantity of pollen that may be floating in the atmosphere at low and high altitudes and the relationship between this quantity and the intensity of his own symptoms. After much experimenting on different methods, he decided on a procedure, of which he wrote: "Ultimately I was led to adopt a simple plan, which I afterwards found was recommended by Dr. Phoebus. This consists in the exposure of slips of glass to the open air for a given length of time, so as to allow any solid matter the air may contain to deposit upon the glass. Each slip of glass had a cell formed upon it with black varnish, so as to enclose a space one centimeter square. This square was coated with a thin layer of fluid prepared for this purpose. [In a footnote he stated that the fluid was made by mixing one part of water, two of proof spirit and one part of glycerine.] After being exposed for twenty-four hours, each slip was placed under the microscope,

and any deposit it contained was carefully examined, and the number of pollen grains counted.”²

Other observations were made by attaching the glass slide to a kite which was flown at elevations of from 500 to 1500 feet. The pollenometric charts made by Blackley in 1866, 1867, and 1869 differ in no essentials from those of today.

In 1925, a half century later, Dr. William Schep-
pergrell of New Orleans, a pioneer student of hay fever, confirmed Blackley’s observations on the pollen content of the upper strata by exposing pollen plates in an airplane at elevations over ten thousand feet¹⁴—studies which have led to the classical aerobiologic observations of O. C. Durham during recent years.

In his lifetime, Blackley, like many pioneers, was looked upon as somewhat of a faddist, and the fact that he practiced homeopathy caused his contemporaries to overlook his brilliant contribution to knowledge of the clinical aspects of allergy, thus again retarding development in this field by almost half a century.

The first noteworthy American contribution to knowledge of hay fever was made by Morrill Wyman of Cambridge, Massachusetts. With some members of his family he had been a lifelong sufferer of an autumnal form of the disease. In 1854, Wyman described the disease in his lectures at the Medical School of Harvard University, where he served for many years as Hersey Professor of the Theory and Practice of Medicine, a title which is still held by present incumbents of this position. In 1872, he published an exhaustive monograph on Autumnal Catarrh, the earliest contribution in the literature on ragweed hay fever. Of his experiment with ragweed, Wyman wrote: “Early in September 1870. I gathered in my grounds at Cambridge, Massachusetts, some Roman wormwood (*Ambrosia artemisiaefolia*) in full flower, covered with pollen, taking the whole plant, stalks and roots. This was carried to the White Mountain Glen, about 1,200 feet above tide, where we remained till September 23 in the afternoon. The parcel containing it was then opened and freely sniffed by myself and son. We were both seized with sneezing and itching of the nose, eyes, and throat, with a limpid discharge. My nostrils were stuffed and my uvula swollen, without cough, but with the other symptoms of autumnal catarrh. These troubles continued through the night, and did not disappear till the afternoon following. Professor Jeffries Wyman (Professor of Anatomy in Harvard University), who was of the same party, but did not sniff the plant, had none of the symptoms just described.”¹⁸

That pollen was an etiologic factor in hay fever, as was so ably established by the experiments of

Blackley and Wyman, was by no means generally accepted in Europe and the United States, despite the established position of Wyman and the high regard in which he was held by his contemporaries. The reports by Blackley and Wyman were published at the beginning of the bacteriologic era—at a time when, owing to the influence of the researches of Pasteur and Koch, hay fever began to be considered an infectious disease. This theory found many adherents, although not one of Koch’s postulates had been fulfilled in any of the experiments described.

In 1876, another monograph on hay fever appeared. It was written by Dr. George M. Beard, a well-known neurologist of New York City, a fellow of the New York Academy of Neurology and of the American Neurological Association. Beard, although well acquainted with the experimental researches of Blackley and Wyman, nevertheless concluded that the whole question of the origin and nature of hay fever was as yet an open one. He advanced the view that the disease, as well as the asthma which is frequently a complication, is essentially a neurosis—a concept of some importance in view of the stress placed in recent years on the psychogenic aspect of allergic manifestations. Owing to the great influence of Beard’s writings on his contemporaries, more than a quarter of a century was to elapse before the significance, of Blackley’s and Wyman’s work was fully appreciated.

VON PIRQUET AND THE FOLLOWING HALF-CENTURY

No historical review of the beginning of the present clinical concept of allergic manifestations would be complete without a brief sketch of the introduction of the skin test, which has so dominated the clinical approach to allergic diseases during the past fifty years. In 1906, Clemens von Pirquet, professor of pediatrics at the University of Vienna, who had acquired an international reputation for his classical work on serum disease, vaccination, and tuberculosis, suggested the term *allergy* for the changed reactivity of the organism following the repeated introduction of pathogenic substances. These studies led to the development of the tuberculin test, which was not only a new diagnostic method for the study of tuberculosis in childhood, but paved the way for the study of the pathogenesis of many other diseases and particularly those of allergic origin.

In 1909, the von Pirquet scarification technique was used by Henry Lee Smith¹⁷ in the study of a patient sensitive to buckwheat, which he published under the title, “Buckwheat-Poisoning.” When Smith reported this case at a meeting of the Johns Hopkins Medical Society, those who were students in the Johns Hopkins Medical School at the time (the author among them) little realized that this case

report opened a new approach to the diagnosis of allergic diseases. Smith not only obtained a positive reaction to a scratch test with buckwheat but produced a constitutional reaction in the patient. Dr. William S. Thayer, clinical professor of medicine at Johns Hopkins at that time, who suggested the test, Dr. Rufus Cole, later director of the Rockefeller Hospital, and Dr. Smith served as controls. In them the application of buckwheat to the scarified skin gave negative results.

The skin test as employed by Smith soon stimulated many other similar studies in this country. In fact, it may be claimed that the skin test as a diagnostic procedure in allergic diseases is essentially an American contribution.

In 1912, O. M. Schloss¹⁵ used the cutaneous test in his studies on children sensitive to common foods, and a year later Clowes⁶ obtained positive skin reactions in ragweed-sensitive patients. This pioneer work was followed by the studies of Goodale¹⁰ who tested asthmatic persons who were sensitive not only to pollens but to horse dander; and Goodale's observations stimulated the extensive research on asthma carried out by I. Chandler Walker at the Peter Bent Brigham Hospital in Boston. Walker used the cutaneous test for the diagnostic recognition of a wide variety of allergic conditions owing to sensitivity to inhalants, foods and other allergens.

Other methods of testing for sensitivity soon were suggested. Smith had thought of testing buckwheat-sensitive patients by the conjunctival route, but at the suggestion of Thayer the cutaneous test was substituted. And Goodale was among the first to obtain mucous membrane reactions by the direct application of pollen extracts. Intracutaneous testing had been used by W. L. Moss at the Johns Hopkins Hospital preliminary to the administration of therapeutic sera, but the first employment of the intracutaneous technique in general allergic diagnosis is usually credited to Robert A. Cooke of New York City.

In 1911, Leonard Noon, working in Sir Almroth Wright's laboratory at St. Mary's Hospital in London, published a paper in the *Lancet* entitled, "Prophylactic Inoculation Against Hay Fever."¹² Noon, who died when but thirty-five years of age, had already achieved a reputation for his researches on tetanus toxin and antitoxin and other contributions to immunology, but it is for his pioneer work on the treatment of hay fever that he is best known to students of allergy. His name will continue in bright usage so long as the Noon unit for measuring pollen dosage remains the most practical method of measurement. It is of historical interest, however, that Karl Koessler, working at the Sprague Institute in Chicago, had anticipated Noon's work. In an article

on "The Specific Treatment of Hay Fever (Pollen Disease)," published in Forchheimer's *Therapeutics of Internal Diseases*, Koessler wrote: "In May 1910, unaware of the work on this subject done in A. E. Wright's laboratory, I began active immunization against hay fever, and thus far I have treated forty-one patients by this method."¹¹

Stimulated by the work of Noon which was later continued by John Freeman of London and Koessler in this country, numerous botanical surveys of hay fever producing plants were begun and extended to almost every region of the United States. Among the earliest of these surveys, and one of particular interest to students of allergy in California, was one carried out by Harvey M. Hall, formerly of the Department of Botany, University of California, and published in the Public Health Reports of the U. S. Public Health Service in 1922. This work was stimulated by the late Dr. Grant Selfridge, a San Francisco otolaryngologist, who in 1918 published one of the earliest reports in California on pollen desensitization.¹⁶ Those who knew Dr. Selfridge, the author included, were impressed by his scientific curiosity, particularly since his training was essentially that of a surgical specialist.

With the publication of the successful therapeutic results in hay fever, the development of clinical applications of the accumulating lore of allergy proceeded at a great pace and many other allergic manifestations were treated by similar methods.

A. F. Coca and Robert A. Cooke contributed much to knowledge of the immune mechanism underlying allergic phenomena and the control of allergic disease by desensitization or, as they preferred to designate it, hyposensitization. Their studies, as well as those of W. W. Duke of Kansas City and Warren T. Vaughan of Richmond, Virginia, were among the first to stress the role played by other allergenic substances than pollen as a cause of allergic manifestations. Duke was the author of the first complete textbook on allergy published in this country.⁸ The first edition appeared in 1925 under the title "Allergy, Asthma, Hay Fever, Urticaria and Allied Manifestations" and contained observations on the importance of foods, drugs and physical agents in allergic diseases. To Vaughan¹⁹ clinical allergists are indebted for many pioneer investigations on other allergic conditions, such as migraine, and for his botanical classification of foods. His concept of allergic equilibrium has helped to explain some puzzling problems in the interpretation of symptoms of allergic origin.

Noon referred to his method of treatment as "prophylactic inoculation," and Koessler used the terms "specific treatment" and "active immunization." Despite the intensive research on the mech-

anism of desensitization during the past twenty-five years begun by Coca and Cooke, and since then extended by a host of workers, there is as yet no acceptable explanation of the mechanism underlying the allergic reaction and its control. The concept suggested by Dale and Laidlaw⁷ in 1910, that histamine may be a participating factor in anaphylaxis, was soon used to explain the basis of allergic manifestations in man, a view which was greatly strengthened by the observations of Duke in 1923 and 1924 on urticaria caused by physical agents. The concept of allergy due to physical agents suggested by him has led to many investigations on the role of excessive histamine formation as a cause of allergic phenomena. These studies have stimulated investigations on many therapeutic methods designed to control excessive histamine release in the tissues of allergic persons. However, neither the use of histaminase, the anti-enzyme of histamine, nor desensitization against histamine has proved effective.

Whereas the introduction of the hormones, cortisone and corticotropin (ACTH) have dwarfed the many advances in the drug therapy of allergic diseases made during the past twenty-five years, no historical sketch would be complete without brief mention of other drugs which have been found helpful. Epinephrine, first isolated by Takamine in 1901 and later by Abel of Johns Hopkins, has been since its first use in asthma during the first decade of this century one of the most potent weapons. And when the experimental work of Chen⁵ and co-workers in 1926 proved the value in bronchial asthma of the alkaloid, ephedrine, isolated from a Chinese plant, Ma Huang, by Nagai in 1887, search was stimulated for other sympathomimetic drugs and the search has continued to the present day.

About a decade ago, another drug was added to the therapeutic armamentarium. Although Askanazy, as early as 1895, found that the salt of theophyllin produced beneficial effects in angina pectoris, its usefulness in combination with ethylene diamine, as aminophylline, was not fully recognized until the year 1940.

The addition of two other groups of useful drugs in the management of allergic patients is so recent as to require only brief mention. Their future place in the treatment of allergic diseases must await the verdict of more research and clinical experience. The antihistamine drugs have already proved to be valuable agents in the symptomatic management of patients with allergic disease, and the introduction of the antibiotics has served as a powerful weapon to combat the secondary infections of the respiratory tract that so frequently complicate allergic diseases.

No discovery, however, has so shaken the foundations of present-day ideas of the basic mechanism

of allergic phenomena as the research, during the past several years, on the part played by the pituitary and adrenal glands in human hypersensitiveness. A historical sketch is not the place for a discussion of the role of the corticosteroids in the therapy of allergic diseases. Probably the greatest significance of the introduction of cortisone and corticotropin, remarkable as their effects may be on patients with allergic disease, lies not so much in the therapeutic results achieved as in the stimulus to basic research on the immunochemical mechanisms underlying allergic phenomena and on ways of modifying or perhaps of bringing about profound changes in the allergic constitution and in the adaptive processes so brilliantly postulated by Hans Selye.

There is another straw in the wind, which would appear to indicate that the care of allergic patients is fast passing beyond the period of technicology. The breeze seems to blow toward the ever-increasing appreciation by physicians of the vital part played by psychogenic factors in allergic diseases. Whereas the importance of these factors in such chronic ailments as hypertension, diabetes, peptic ulcer and many other chronic conditions has been fully recognized, little emphasis has been placed on the psychiatric management of patients with allergic disease. Many contributions to the literature on this phase of therapy have appeared in recent years, but considerable resistance has been shown by allergists to the adoption of psychotherapeutic methods. This aversion may owe (as Ross and Wilson pointed out in their chapter on Psychotherapy in Bronchial Asthma, published in Abramson's text on the Somatic and Psychiatric Treatment of Asthma¹) to overemphasis placed by allergists on organic factors, and by psychiatrists on psychogenic factors. It is probable that either of these factors alone or both synergistically can act as trigger mechanisms in giving rise to allergic manifestations. In some instances symptoms may result from allergic causes alone, in others from psychogenic factors, but perhaps in the majority of instances both allergic and psychogenic mechanisms serve to bring about and prolong allergic manifestations. It would appear, therefore, that allergists of the future will need to devote more time to the psychotherapeutic as well as to organic factors in the management of patients.

Furthermore, the training of the next generation of physicians specializing in allergy will be influenced, in no small measure, by the ever-expanding horizons which in recent years have removed diagnosis and treatment of allergic disease from its limited technological confines. This trend will of necessity greatly influence not only the kind of undergraduate instruction in allergic diseases given in medical schools but also the planning of post-

graduate teaching. The postgraduate instructional courses on the many facets of allergy presented both by the American Academy of Allergy and the American College of Allergists fill a great need, and these organizations are to be commended for the vigor with which they have carried out this part of their program. However, there still remains some difference of opinion as to how instruction in allergy should be planned on the undergraduate level, and under whose aegis certification of the allergists should be placed.

It is common knowledge that undergraduate instruction in allergy in medical schools has lagged in spite of the fact that allergic phenomena constitute an essential part of the basic sciences of immunology, bacteriology, physiology, pathology, pharmacology, endocrinology and immunochemistry. Those who have had the responsibility of teaching medical students the fundamentals of allergy have been impressed with the immensity of the task of presenting adequately a subject which has such wide ramifications. It has become the conviction of many teachers of this subject that undergraduate instruction in allergy can be given most effectively as part of the teaching of the individual basic science. Thus a course in immunology or immunochemistry should include a discussion of sensitization in experimental animals and in man, and the fundamentals of the mechanism involved both in anaphylaxis as well as in human hypersensitiveness. The physiologist and pathologist could devote some time to the physiologic and pathologic aspects of the allergic reaction, and the pharmacologist to an evaluation of the common sympathomimetic drugs, antihistamines and the newer hormones, in the drug therapy of allergic diseases.

In brief, undergraduate teaching in allergy should be made a part of the instruction in the basic medical sciences. These basic facts and theories can then be coordinated with the common clinical manifestations of allergy such as hay fever, asthma, eczema, urticaria, gastrointestinal distress and allergic reaction to drugs. This integration of the subject can best be carried out in the out-patient allergy clinic by a member of the clinical staff adequately trained in this branch of internal medicine. Such a plan would lessen the trend, now so prevalent, toward overburdening the medical curriculum with instruction in the subspecialties. It must be admitted, however, that this is contrary to the program of the American Academy of Allergy and the American College of Allergists. Both of these organizations are on record as sponsoring undergraduate lecture courses in this specialty.

Closely related to the problem of undergraduate and graduate instruction in allergy is that of certifi-

cation. In 1948, a joint committee representing the American Academy of Allergy and the American College of Allergists adopted a resolution²⁰ recommending the establishment of an independent or autonomous board. It is the conviction of many, however, that certification in allergy should continue to be the function of the boards of Internal Medicine and Pediatrics. The creation of an independent board might stunt rather than advance progress in knowledge of allergy, because it would deprive this subspecialty of the sustenance from the mother trunk upon which its growth must depend, and without which the dependent branches would undergo gradual atrophy.

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